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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,417	01/17/2002	David Harrow Gelfand	022101-000320US	4095

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EXAMINER

SITTON, JEHANNE SOUAYA

ART UNIT	PAPER NUMBER
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1634

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/052,417

Applicant(s)

GELFAND ET AL.

Examiner

Jehanne S. Sitton

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 August 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 6-8, 11-13, 16-18, 21-23, 26, 27, 31-36, 39-42, 45-47 and 50-52 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 6-8, 11-13, 16-18, 21-23, 26-27, 31-36, 39-42, 45-47, and 50-52 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Currently, claims 1-3, 6-8, 11-13, 16-18, 21-23, 26-27, 31-36, 39-42, 45-47, and 50-52 are pending in the instant application. The amendments and arguments have been thoroughly reviewed but are insufficient to place the instant application in condition for allowance. The following rejections constitute the complete set being presently applied to the instantly pending claims. The following office action contains new grounds of rejection under obviousness type double patenting, accordingly, this action is NON-FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

New Grounds of Rejection

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3, 6-8, 11-13, 16-18, 33-36, 39-42, 45-47, 50-52 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims do not distinguish over polypeptides and nucleic acids as they exist naturally because the claims do not particularly point out any non naturally occurring differences between the claimed products and naturally occurring ones. In the absence of the hand of man, the naturally occurring products are considered non statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor.

Claim Rejections - 35 USC § 112

4. Claims 1-3, 6-8, 11-13, 16-18, 21-23, 26-27, 31-36, 39-42, 45-47, and 50-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter Rejection.

The claims have been amended to recite the limitation: wherein said polymerase is selected from a *Thermus* species other than *Thermus aquaticus*. The response provides Table 1 of the specification as support for the amendment. The specification has been thoroughly reviewed. However, the specification does not appear to provide support for any *Thermus* species other than *Thermus aquaticus*. At page 15, table 1, the specification provides support for the following *Thermus* species: *flavus*, *thermophilus*, *specie Z05*, *Specie sps17*, *caldphilus*, and *filformis*, however the claims as amended now encompass additional *Thermus* species which have not been taught or described by the specification, including *T. scotodocus*, *T. osimai*, *T. brockianus*, *T. igniterrae*, and *T. antranaikianii*. Accordingly, the amendment appears to have introduced new matter into the claims. This rejection can be overcome by reciting instead “wherein the polymerase is from a *Thermus* species selected from the group consisting of *T. flavus*, *T. thermophilus*, *T. specie Z05*, *T. Specie sps17*, *T. caldphilus*, and *T. filformis*.”

Claim Rejections - 35 USC § 102

5. Claims 1-3, 6-8, 11-13, 16-18, 21-23, 26-27, 31, 33-36, 39-42, and 45-47 are rejected under 35 USC 102(e) as being anticipated by Brandis I (Brandis et al; US Patent 6,265,193).

Brandis I teaches and claims mutant DNA polymerases having at least one mutation at position 681 with respect to *Taq* DNA polymerase, wherein the mutant DNA polymerase has at least 2 fold reduced discrimination against the incorporation of a fluorescein type dye labeled nucleotide as compared to a naturally occurring DNA polymerase (see claims 1-13, col. 6, lines 4-39, col. 8, Tables 1 and 2 at cols 17-22).

With regard to claims 1-3, 6-8, 33-36, 39-42, and 45-47, Brandis I teaches making the specific mutants in *Taq* polymerase, which comprises SEQ ID NOS 1-3, as acknowledged by the instant specification at page 15, Brandis I teaches making a number of mutants at position 681 of *Taq*, which have at least 3 fold lower discrimination (table 2, cols 21-22). Brandis teaches making the specific E681K mutant. Brandis I teaches kits comprising the mutant polymerase and a fluorescently labeled nucleotide dye (claims 6-9), fluorescein type dyes (col. 4), and nucleotides which are any naturally occurring nucleotides or analogs such as 2',3' dideoxynucleotides (chain terminator) (col. 4, lines 35-39).

With regard to the newly added claim limitation "wherein said polymerase is selected from a *Thermus* species other than *Thermus aquaticus*", Brandis I does not limit the mutant polymerases described to only *Taq*, but also specifically teaches that the mutant polymerases include polymerases from other *Thermus* species including *Thermus flavus* (col. 8, lines 53-54).

With regard to claims 11-13 and 16-18, Brandis I teaches providing polynucleotides encoding the mutant polymerases (abstract, all of col. 11, especially lines 40-45).

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With regard to claims 21-23, 26-27, and 31 Brandis I teaches to use the mutant polymerases in methods of Sanger sequencing such as dideoxy nucleotide chain termination, PCR, polynucleotide labeling, and minisequencing.

6. Claims 1-3, 6-8, 11-13, 16-18, 21-23, 26-27, 31, 33-36, 39-42, and 45-47 are rejected under 35 USC 102(e) as being anticipated by Brandis II (Brandis et al; US PreGrant Publication 2002/0164591) or Brandis III (Brandis et al; US PreGrant Publication 2006/0088879).

Brandis II and III each teaches and claims mutant DNA polymerases having at least one mutation at position 681 with respect to Taq DNA polymerase, wherein the mutant DNA polymerase has at least 2 fold reduced discrimination against the incorporation of a fluorescein type dye labeled nucleotide as compared to a naturally occurring DNA polymerase (see claims 1-8, 15, Tables 1 and 2). With regard to the newly added claim limitation “wherein said polymerase is selected from a *Thermus* species other than *Thermus aquaticus*”, Brandis II and III do not limit the mutant polymerases described to only *Taq*, but also specifically teaches that the mutant polymerases include polymerases from other *Thermus* species including *Thermus flavus* (para 0037).

With regard to claims 1-3, 6-8, 33-36, 39-42, and 45-47, Brandis II and III each teaches making the specific mutants in Taq polymerase, which comprises SEQ ID NOS 1-3, as acknowledged by the instant specification at page 15. Brandis II and III each teaches making a number of mutants at position 681 of Taq, which have at least 3 fold lower discrimination (table 2,). Brandis teaches making the specific E681K mutant. Brandis II and III each teaches kits comprising the mutant polymerase and a fluorescently labeled nucleotide dye, fluorescein type

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dyes, and nucleotides which are any naturally occurring nucleotides or analogs such as 2',3' dideoxynucleotides (chain terminator).

With regard to claims 11-13 and 16-18, Brandis II and III each teaches providing polynucleotides encoding the mutant polymerases (abstract, claim 9 of Brandis II)

With regard to claims 21-23, 26-27, and 31 Brandis II teaches to use the mutant polymerases in methods of Sanger sequencing such as dideoxy nucleotide chain termination, PCR, polynucleotide labeling, and minisequencing.

Claim Rejections - 35 USC § 103

7. Claims 32 and 50-52 are rejected under 35 USC 103(a) as being unpatentable over Brandis I, II, or III each in view of Gelfand (US Patent 5,939,292).

Brandis I, II, and III teach mutant DNA polymerases having at least one mutation at position 681 with respect to Taq DNA polymerase, wherein the mutant DNA polymerase has at least 2 fold reduced discrimination against the incorporation of a fluorescein type dye labeled nucleotide as compared to a naturally occurring DNA polymerase. Brandis I, II, and III teach making the specific E681K mutant. Brandis I, II, and III teach kits comprising the mutant polymerase and a fluorescently labeled nucleotide dye, fluorescein type dyes, and nucleotides which are any naturally occurring nucleotides (encompasses dNTP and rNTP). With regard to the newly added claim limitation "wherein said polymerase is selected from a *Thermus* species other than *Thermus aquaticus*", Brandis I, II and III do not limit the mutant polymerases described to only *Taq*, but also specifically teaches that the mutant polymerases include

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polymerases from other *Thermus* species including *Thermus flavus* (col. 8 lines 53-54 of Brandis I; para 0037 of Brandis II and III).

With regard to claims 32 and 50-52, Brandis I, II and III teach to provide mutant polymerases comprising other mutations in addition to the discrimination mutations such as those at position 681 of Taq polymerase, including mutants outside the discrimination regions (col. 10, lines 9-23, Table 2, cols 19-22). Brandis I, II and III teach mutations at position 615 of Taq polymerase (instant SEQ ID NOS 18). Brandis I, II or III do not specifically teach a polymerase comprising *both* a mutation at position 681 and a mutation at position 615, however Gelfand teaches to use modified DNA polymerases with enhanced efficiency for incorporating unconventional nucleotides, such as ribonucleotides, using a polymerase with a mutation at position 615, corresponding to Taq polymerase, in methods of DNA sequencing (see abstract, cols 2-3). Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to provide a mutant DNA polymerase with both a mutation at position 681 and 615, relative to Taq, both taught by Brandis, in the mutant polymerases of Brandis I, II or III for use in the sequencing methods or primer extension (minisequencing) methods taught by Brandis I, II or III because Gelfand teaches that the mutation at position 615 in a DNA polymerase provides for DNA polymerases that enable alternative nucleic acid synthesis methods for accurate and cost effective nucleic acid DNA sequence analysis. It would have further been prima facie obvious to the ordinary artisan at the time the invention was made to provide such mutant polymerases and a ribonucleotide labeled with a fluorescein type family dye for the purposes of making the methods of Brandis I, II or III, each in view of Gelfand more convenient to perform.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claim 31 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13-16, 20-24, 27-32, 36-44 and 48-52 of copending Application No. 09/823,649 in view of Giardano (US Patent 6,107,029).

Claim 31 is drawn to a method of producing labeled DNA by providing a mutant thermostable DNA polymerase comprising LSX[-E]L[AS]IPXXE, a fluorescein family dye labeled nucleotide and performing a DNA synthesis reaction. The instant specification defines a "DNA synthesis reaction" to encompass PCR, SDA, transcription mediated amplification, primer extension, and reverse transcription.

The claims of the '649 application are directed to methods of reverse transcription using a mutant thermostable polymerase which comprises L[SA]X[-EAGPD][LI][SA]XXXXE and treating a reaction mixture to initiate synthesis of an extension product to provide a cDNA. The

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claims further limit the polymerase to a mutant thermostable polymerase such as *Thermus thermophilus*, which has an I at position 7 and a P at position 8 of instantly claimed SEQ ID NO: 1. Accordingly, it is clear that the mutant polymerases in the instant claims and the claims of the '649 application are coextensive in scope. The claims differ in that the claims of the '649 application do not provide for a fluorescein family dye labeled nucleotide, however Giordano teaches that synthesizing labeled cDNA from an RNA molecule allows use of the cDNA to screen a library of genes thought to contain the gene encoding an RNA of interest (see col 10, lines 3-8). Additionally, Giordano teaches the use of labels such as fluorescein dyes (col. 7, lines 15-20). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the DNA synthesis reaction of '649 to label cDNA molecules as taught by Giordano. The ordinary artisan would have been motivated to produce labeled cDNA in the methods of '649 for the purpose of providing cDNA which could be used to screen a library of genes for an RNA of interest as taught by Giordano.

This is a provisional obviousness-type double patenting rejection.

Conclusion

10. No claims are allowed.
11. It is noted that the filing of a declaration under 37 CFR 1.131 cannot be used to swear behind claims directed to subject matter which is claimed by the '193 patent. See MPEP 715 II:

An affidavit or declaration under 37 CFR 1.131 is not appropriate in the following situations:...

(B) Where the reference U.S. patent or U.S. patent application publication claims the same patentable invention. See MPEP § 715.05 for a discussion of "same patentable invention" and MPEP *> Chapter 2300<.

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With regard to claims directed to subject matter claimed in a Publication for Patent, see MPEP 715.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Jehanne Sitton
Primary Examiner
Art Unit 1634

Jehanne Sitton
11/4/07